Carboplatin & gemcitabine
(NSCLC and breast cancer regimen)

Indication
Non-small cell lung cancer Stage III/IV
Advanced breast cancer

Regimen details
Carboplatin AUC5 day 1
Gemcitabine 1250mg/m2 days 1 & 8

Cycle frequency
Every 21 days

Number of cycles
Maximum 6 cycles

Administration
Day 1
Gemcitabine is administered over 30 minutes (longer infusion time may lead to increased toxicity)
Following the gemcitabine, carboplatin is administered in 250-500mL glucose 5% over 30- 60 minutes

Days 8
Gemcitabine administered over 30 minutes (longer infusion time may lead to increased toxicity)

Gemcitabine volume will vary depending on product used

Patients should be observed closely for hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of carboplatin. Facilities for the treatment of hypotension and bronchospasm must be available.
If hypersensitivity reactions occur, minor symptoms such as flushing or localised cutaneous reactions do not require discontinuation of therapy. The infusion may be temporarily interrupted and when symptoms improve restarted at a slower infusion rate. Chlorphenamine 10mg IV may be administered. Severe reactions, such as hypotension, bronchospasm or generalised rash/erythema require immediate discontinuation of carboplatin and appropriate therapy.

Pre-medication
None specific

Emetogenicity
Day 1 – moderate
Day 8 - low

Additional supportive medication
None routinely given

Extravasation
Carboplatin – irritant
Gemcitabine - neutral

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Calcium	14 days
Magnesium	14 days

Investigations –pre subsequent cycles

FBC, U+E (including creatinine), LFT (including AST)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	≥ 1.0 x 10^9/L (but see under "Dose modifications" below)
Platelet count	≥ 100 x 10^9/L (but see under "Dose modifications" below)
Creatinine clearance	≥ 30 mL/min
Bilirubin	≤ 1.5 x ULN
AST	< 1.5 x ULN

Dose modifications

Haematological toxicity

DAY 1

Neutrophils > 1.5	AND	Plat>100	Proceed with full dose
Neutrophils 1.0-1.5			Discuss with consultant
Neutrophils < 1.0	AND/OR	platelets < 100	Defer 1 week

DAY 8

Neutrophils > 1.0	and/or	platelets >100	Proceed with full dose
Neutrophils < 1.0	and/or	platelets <100	Defer

If there has been a dose delay reduce subsequent doses by 20%

Renal impairment

If serum creatinine changes by >20% from previous cycle, consider dose recalculation.

If calculated CrCl improves the dose should not be increased unless there is a clear cause of renal function improvement (such as treatment of urinary tract obstruction)

Hepatic impairment

Use gemcitabine in caution in hepatic impairment.
Raised transaminases do not seem to cause dose limiting toxicity. Transient increases in liver enzymes have been seen in patients being treated with both carboplatin and gemcitabine although no dose reduction is usually required.
If bilirubin > 1.5 x ULN, initiate gemcitabine at dose of 800 mg/m^2.

Neurotoxicity

Grade	Carboplatin dose	Gemcitabine dose
0-1	100%	100%
2	50%	100%
3	Omit	100%
4	Discontinue	Discontinue

Adverse effects –

for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Infertility
Peripheral neuropathy
Hypersensitivity reactions
Haemolytic uraemic anaemia*
Pulmonary fibrosis
Electrolyte disturbances

Gemcitabine should be discontinued at the first sign of microangiopathic haemolytic anaemia (such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevated bilbirubin, creatinine, blood urea nitrogen or LDH. Renal failure may not be reversible with discontinuation of therapy, dialysis may be required.

- **Frequently occurring side effects**

Nausea and vomiting
Mucositis, stomatitis
Diarrhoea, constipation
Oedema

- **Other side effects**

Raised transaminases
Alopecia
Fatigue

Significant drug interactions

– for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: increased or fluctuating anticoagulant effects. Avoid if possible, consider switching patient to a low molecular weight heparin during treatment or if the patient continues taking an oral anticoagulant monitor the INR at least once a week and adjust dose accordingly.

Carboplatin only:
Aminoglycoside antibiotics: increased risk of nephrotoxicity and ototoxicity
Clozapine: increased risk of agranulocytosis, avoid concomitant use
Diuretics: increased risk of nephrotoxicity and ototoxicity
Nephrotoxic drugs: increased nephrotoxicity ; not recommended
Phenytoin: carboplatin reduces absorption and efficacy of phenytoin

Additional comments

Nil

References

SWCN protocol -
http://www.swscn.org.uk/wp/wp-content/uploads/2014/12/Gemcitabine-Carboplatin-NSCLC1.pdf

This protocol has been reviewed by the Lancashire & South Cumbria Lung Oncology Consultants' Group and responsibility for the template lies with the Head of Service

Date: May 2021
Review: May 2023
VERSION: 15